From fundamental science to product: a bottom-up approach to sunscreen development

Natércia d. N. Rodrigues[a*] and Vasilios G. Stavros[a*]

[a]*University of Warwick, Department of Chemistry, Library Road, Coventry, CV4 7AL*

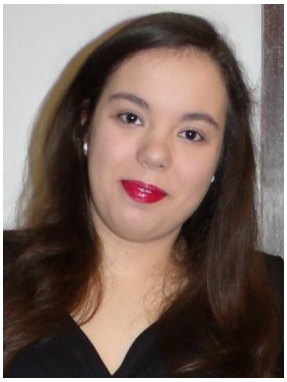
* *Corresponding author:* v.stavros@warwick.ac.uk

* *Corresponding author:* n.das-neves-rodrigues@warwick.ac.uk

Abstract

Despite the pivotal role of ultraviolet (UV) radiation in sustaining life on Earth, overexposure to this type of radiation can have catastrophic effects, such as skin cancer. Sunscreens, the most common form of artificial protection against such harmful effects, absorb UV radiation before it reaches vulnerable skin cells. Absorption of UV radiation prompts ultrafast molecular events in sunscreen molecules which, ideally, would allow for fast and safe dissipation of the excess energy. However, our knowledge of these mechanisms remains limited. In this article, we will review recent advances in the field of ultrafast photodynamics (light induced molecular processes occurring within femtoseconds, fs, 10^{-15} s to picoseconds, ps, 10^{-12} s) of sunscreens. We follow a *bottom-up approach* to common sunscreen active ingredients, analysing any emerging trends from the current literature on the subject. Moreover, we will identify the main questions that remain unanswered, pinpoint some of the main challenges and finally comment on the outlook of this exciting field of research.

Keywords: sunscreens, photophysics, photochemistry, photodynamics, ultrafast laser spectroscopy, time-resolved, ultraviolet, photoprotection



Natércia d. N. Rodrigues

Natércia Rodrigues studied at the University of Leicester, obtaining a MChem degree in 2014. During her undergraduate degree, she undertook a placement year working with the Science and Technology Facilities Council at the Artemis Facility in the Rutherford Appleton Laboratories, Didcot. She is currently a PhD student under the supervision of Professor Vasilios Stavros at the University of Warwick. Her thesis focuses on obtaining a comprehensive understanding of the ultrafast photodynamics of sunscreen molecules in an effort to inform their rational molecular design towards optimised photoprotection.

Vasilios G. Stavros

Vasilios Stavros is a Professor of Physical Chemistry at the University of Warwick. He completed his PhD in 1999 at King's College London, working in the group of Prof. Helen Fielding and remained at King's College for a further three years as an EPSRC postdoctoral research fellow. In 2002, he undertook a postdoctoral position at the University of California Berkeley, working for Prof. Stephen Leone. He returned to the UK in 2005 as a Royal Society University Research Fellow. His research is centred on understanding photoprotection and photoactivation mechanisms in biologically related molecules using both gas- and solution-phase pump–probe spectroscopies.

1. Introduction: Sun, Skin and Sunscreens

Ultraviolet (UV) radiation from the Sun is categorised as UVC (100 – 280 nm), UVB (280 – 315 nm) and UVA (315 – 400 nm).[1,2] Stratospheric ozone prevents any significant amount of highly destructive UVC radiation from reaching the Earth's surface, as well as absorbing a significant portion of UVB radiation.[1] The UV radiation at the Earth's surface is, therefore, composed mostly of UVB and UVA radiation, the combined total of these accounting for approximately 3.4 % of the total atmosphere attenuated solar spectrum (*c.f.* 8 % before the atmosphere, see Figure 1).[2-4]

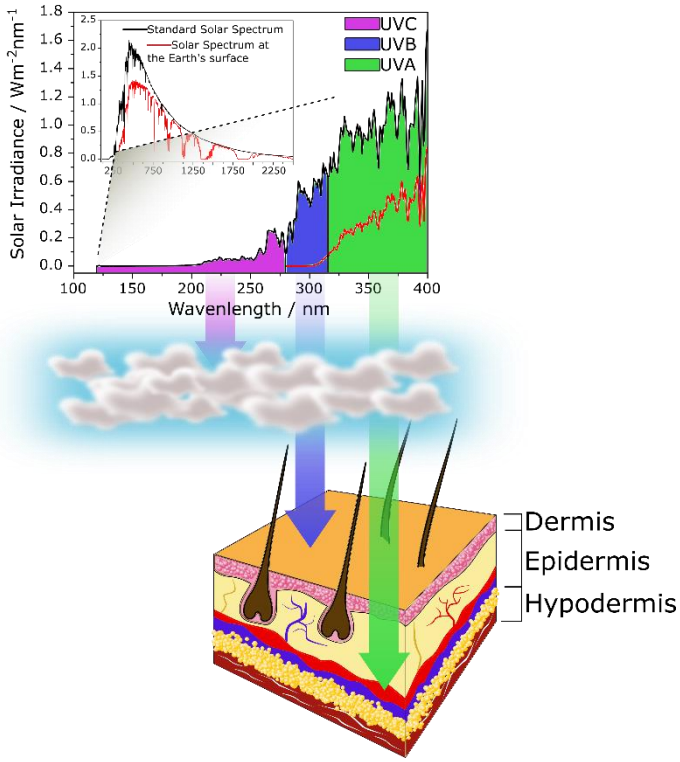
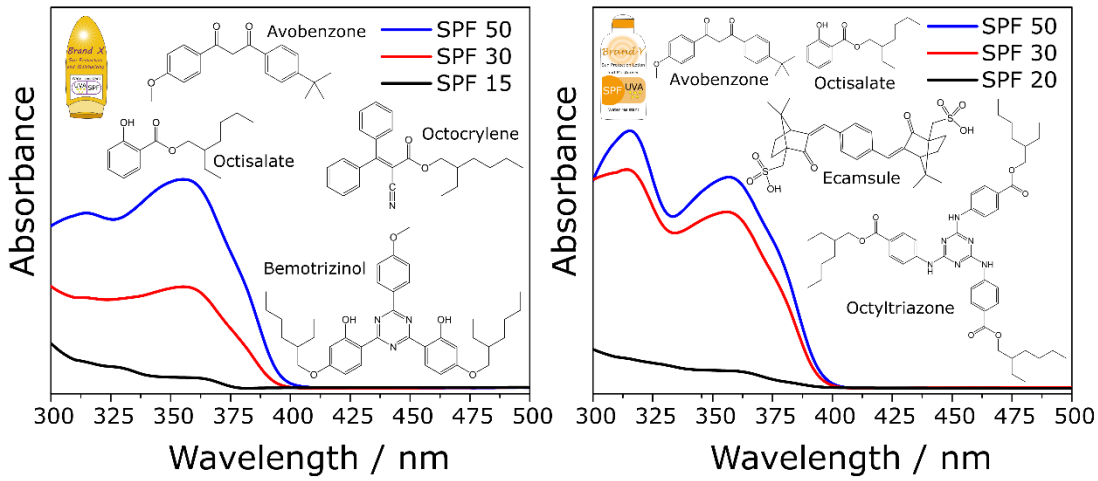


Figure 1: (Top) The plot of solar irradiance *vs.* wavelength shows the solar spectrum before and after the Earth's atmosphere (black and red lines, respectively). Shaded areas are for illustrative purposes only. Solar spectra adapted from reference 4. (Bottom) A representation of the interaction between the different types of UV radiation and the skin: UVC (purple arrow) is mostly absorbed/scattered/reflected by the atmosphere and hence its presence at the surface of the skin is negligible; UVB (blue arrow) reaches the skin's dermis and UVA (green arrow) penetrates deeper into the skin, reaching the epidermis.

The UV radiation provided by the Sun plays a crucial role in sustaining life on Earth. When UV photons are absorbed by key chromophores in biological systems, these light absorbing molecules are left in excited states with enough energy to undergo chemical reactions. Such photoinduced chemistry, otherwise termed *photochemistry*, is the trigger for photosynthesis, for example, the unique biological process which converts the energy from sunlight into the biochemical energy necessary to sustain life on Earth.[5] In humans, one of the most important UV-induced processes is the production of vitamin D,[6,7] which is best known for its ability to protect against musculoskeletal disorders[6] but has also been found to provide protection against infectious, autoimmune and cardiovascular diseases.[8]

The extensive benefits of UV radiation to life are heavily counterbalanced by the serious consequences of excess exposure to this type of radiation. In plants, excess UV radiation disrupts photosynthetic processes, as well as reducing carbon dioxide fixation and oxygen evolution.[9,10] For humans, it is now firmly established that overexposure to UV radiation is related to erythema (sunburn), skin aging and carcinogenesis – namely, it is related to melanoma, one of the most aggressive human cancers.[11,12] As shown in Figure 1, UVB and UVA interact differently with the human skin, and their effects can also be quite distinct. UVB radiation is readily absorbed by DNA and can thus cause alterations to the genetic sequence which, if unrepaired by excision repair pathways,[13] may eventually lead to cancer.[14,15] In comparison, UVA has been extensively reported to produce harmful levels of reactive oxygen species (ROS) in the skin, which is a major factor contributing to both carcinogenesis and skin aging *via* oxidative stress pathways.[16,17] The human body defends itself against such radiative stress by producing melanin pigments which absorb harmful radiation before it reaches DNA.[18] The production of melanin – melanogenesis or, as it is more commonly known, tanning – is triggered by exposure to UV radiation. However, this is a delayed response and it may take 3-5 days for any significant protection to be afforded by the extra melanin produced.[19] Any photodamage occurring before the skin is sufficiently protected may have a catastrophic effect on the skin.

Today, the deficiencies of melanin photoprotection are supplemented by artificial photoprotection, mainly in the form of photoprotective lotions, *i.e.* sunscreens.[20] Commercial sunscreen lotions are complex mixtures of UV absorbers (herein termed sunscreen molecules) and stabilisers, solvents, emollients, film structure enhancers and cosmetic adjuncts. Currently, sunscreens are required by the relevant regulatory agencies (such as the United States Food and Drug Administration or the European Commission) to provide protection against both UVA and UVB radiation.[20-22] In broad terms, sunscreen photoprotective efficacy is measured in terms of sun protecting factor (SPF) for UVB and *critical wavelength* for UVA.[20] SPF values are a dimensionless ratio between the radiation dosage required to cause erythema in sunscreen protected *vs.* unprotected skin;[20] Figure 2 demonstrates how absorbance varies with SPF values and gives a list of the current globally approved sunscreen molecules.[20] The *critical wavelength*, which is the wavelength at which 90 % of the integrated UV absorbance is reached (from 290 nm to 400 nm), should be longer than 370 nm and provides a measure of the broad-spectrum character of the sunscreen product.[20,23] Current sunscreen testing methods are carried out *in vitro* and hence may not accurately represent the efficacy of the sunscreen when on the skin. Moreover, *in vitro* tests use an application dose of 2 mg/cm^2 when, in reality, consumer application doses vary between 0.5-1.0 mg/cm^2.[20]



Globally Approved Sunscreens		
Protection range	Sunscreen name	Trade name
UVB	Oxybenzone	Uvinul® M40
	Sulisobenzone	Uvinul® MS40
	Octinoxate	Uvinul® MC 80
	Octisalate	Neo Heliopan® OS
	Homosalate	Eusolex® HMS
	Octocrylene	Uvinul® N 539 T
	Ensulizole	Eusolex® 232
	Titanium Dioxide	Eusolex® T2000
	Iscotrizinol	Uvasorb HEB
	Octyltriazone	Uvinul® T150
	Amiloxate	Neo Heliopan® E1000
	Enzacamene	Eusolex® 6300
UVA	Avobenzone	Parsol® 1789
	Zinc Oxide	Z-Cote® HP1
	Bemotrizinol	Tinosorb® S
	Bisoctrizole	Tinosorb® M
	Ecamsule	Mexoryl® SX
	Drometrizole	Mexoryl® XL

Figure 2: Absorbance spectra of alcohol extractions of two commercial sunscreens with different advertised SPF values: 15/20 (black line), 30 (red line) and 50 (blue line). Each plot also shows some of the active ingredients responsible for the observed absorbance for each respective sunscreen. Note: molecular structures of these active ingredients were randomly placed on the plot and their positions relative to the wavelength axis *does not* reflect their absorption regions. The absorbance spectra observed are a result of a mixture of active ingredients. These spectra were obtained by second year chemistry students at the University of Warwick as part of a laboratory activity using the extraction methodology described by Abney and Scalettar.[24] A list of the globally approved sunscreens currently on the market is also presented in tabulated form, adapted from reference 20.

The most fundamental requirements of an ideal sunscreen molecule are that it strongly absorbs UVB/UVA radiation and poses no risk to human health or the environment.[25] Moreover, the sunscreen lotion should be easily applied, have a pleasant odour and a pleasant on-skin appearance and texture, so that consumers are more likely to comply with sunscreen application guidelines, thus improving overall protection. However, an aspect that is currently not widely considered in sunscreen development is the molecular level behaviour of sunscreen molecules immediately after absorption of UV radiation. The molecular events triggered by absorption of UV radiation typically occur within an ultrafast timescale – femtoseconds (fs) to picoseconds (ps), 10^{-15} s to 10^{-12} s, respectively – and constitute the sunscreens molecule's ultrafast photophysics and/or photochemistry, termed jointly as *photodynamics*. Sunscreen molecules may undergo a number of photodynamical processes to dissipate the excess energy resulting from absorption of UV radiation, a summary of which is given in Figure 3.[4,20,26,27] In an ideal sunscreen molecule, these photodynamic processes should allow for dissipation of excess energy as harmless heat, without loss of molecular integrity and without generating reactive photoproducts such as ROS; this sunscreen would then be said to be *photostable*.[28]

However, the excited states of ideal sunscreens should also be short-lived, *i.e.* the ideal sunscreen agent should dissipate excess energy as harmless heat and return to its original form – its ground electronic energy level – before the excited state has the chance to undergo undesirable chemistry with (or energy transfer to) other components of the sunscreen formulation or even with the skin itself.[29] To fulfil all of these requirements – a strong UVB/UVA absorber that dissipates energy safely and effectively, and can be easily incorporated in aesthetically pleasing sunscreen formulations – is often challenging and never achieved with a single sunscreen molecule. Hence the need for sunscreen lotions to be, in fact, complex mixtures of UV absorbers as well as components to ensure stability, pleasurable fragrance and texture, *etc.*

The lack of suitable filters for certain wavelengths and possible degradation of sunscreen molecules after exposure to UV radiation are some of the challenges currently facing the sunscreen industry.[20,28] A rational molecular design may address these challenges by allowing the development of sunscreen molecules tailor-made for optimised photoprotection.[29,30] First of all, it is necessary that the ultrafast photodynamics of a

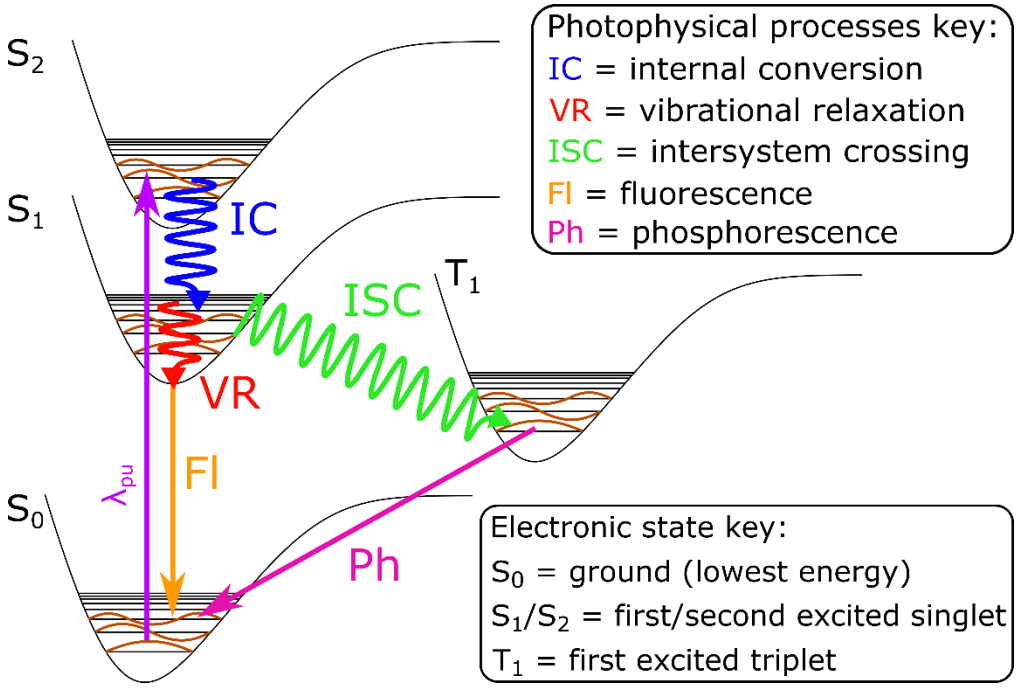


Figure 3: Simplified Jablonski diagram demonstrating several non-dissociative photophysical processes by which absorbed energy (λ_{pu}) may be dissipated. Internal conversion (blue), vibrational relaxation (red) and intersystem crossing (green) are non-radiative decay pathways, typically occurring within the picosecond (or less) timescale. Intersystem crossing, however, being a forbidden transition, may occur over several hundreds of ps or longer. Fluorescence and phosphorescence, on the other hand, are radiative decay pathways and may take place within several seconds (especially phosphorescence). Note: vibrational relaxation in vacuum is achieved *via* redistribution of energy amongst vibrational levels; in solution, the energy may be transferred to the solvent.

sunscreen molecule are clearly established. A comprehensive understanding of photoprotective mechanisms of action may then inform molecular structure manipulation of sunscreen molecules in order to enhance energy redistribution mechanisms or hinder relaxation pathways that may lead to undesirable side chemistry (such as degradation) or energy transfer to other components of the sunscreen formulation or the skin itself. Since sunscreen molecules are used as part of complex sunscreen formulations, it is also important to understand how these UV-induced processes are affected by environmental factors. This article provides a review of recent studies which employed ultrafast laser spectroscopy techniques to further our understanding of ultrafast sunscreen photodynamics. In particular, this article will explore any trends identified thus far, in terms of preferred photoprotective mechanisms and how such mechanisms are affected by molecular structure or environmental factors. We will conclude by aiming to place the current findings in the context of the sunscreen industry and suggesting further work necessary for advancing the pursuit for optimum photoprotection.

2. Mapping Ultrafast Photodynamics

Laser femtochemistry, as defined by its creator and Nobel Prize laureate Ahmed H. Zewail, is the field of science which is *"concerned with the very act of the molecular motion that brings about chemistry (…) on the femtosecond (…) timescale"*.[31] The time resolution necessary to map the complete evolution of a chemical event at a molecular level within such a short timescale can only be achieved by employing ultrashort laser pulses and pump-probe techniques. In such experiments, two laser pulses are utilised: the pump, of wavelength λ_{pu}, photoexcites the molecule under study to the excited state of interest; one probe pulse then follows at each one of several pump-probe time delays, Δt, to monitor the evolution of the system after photoexcitation. The detection methods used to monitor the evolution of the system are varied, as will be discussed later in this section. Pump-probe techniques thus allow for molecular events to be monitored from time zero (*i.e.* the point in time at which the pump and probe laser pulses arrive at the sample simultaneously, $\Delta t = 0$ or t_0), through any transition states and, ultimately, to the system's final state. This approach can be applied in many different ways to map chemical events in both the gas- and condensed-phase (in vacuum and in solution, respectively). Such techniques have been described in much detail before[4,27] and will only be summarised here.

a. In vacuum

Sample preparation for state-of-the-art ultrafast laser spectroscopy techniques in vacuum commonly involves the production of a molecular beam: a directed flow of vibrationally cold molecules created by expanding a high pressure gaseous mixture of an inert gas seeded with the molecule of interest through a small orifice into a vacuum.[32] Following the aforementioned pump-probe experimental design, represented diagrammatically in Figure 4, this molecular beam of isolated molecules is made to interact with the pump laser pulse, which photoexcites these molecules, followed by a probe laser pulse that ionises the photoexcited molecules. *Time-resolved ion yield* (TR-IY) detects the ions resulting from the probe step (be it the molecular or any fragment ions). As the excited state population decays, the resulting changes to ion signal are recorded and thus the evolution of the system as a function of Δt is monitored. In a similar fashion, electrons may be monitored instead, in which case the technique is referred to as *time-resolved photoelectron spectroscopy* (TR-PES).

One of the detection methods used in gas-phase ultrafast laser spectroscopy techniques is time-of-flight (TOF) mass spectrometry, which relies on the different flight times of different mass-to-charge ratio (*m/z*) molecular fragments (ions) for a fixed flight length. After acceleration, away from the region of interaction between the molecular and laser beams, charged photoproducts enter a force-free flight zone where they are separated according to *m/z*, *i.e.* heavier fragments will travel slower and hence will reach the detector later than lighter fragments. The detector is usually a set of micro-channel plates (MCPs) which create an electron cascade for each charged particle that collides with the MCP surface. The resulting current is measured with, for example, an oscilloscope and the evolution of each mass channel (corresponding to each *m/z* fragment) can be monitored as a function of Δt.

Within a molecular beam, reactions are assumed to be unimolecular, *i.e.* the observed photodynamics are assumed to follow first order kinetics. Therefore, the transients resulting from monitoring a mass channel at several Δt can be described as an exponential rise or decay, or a sum of exponentials if more than one pathway is accessible. Fitting the data with such a kinetic model yields the time constants, τ, for each process, where $\tau = {}^{1}/_{k}$ with k being the rate constant for each pathway. Both the excited state lifetimes of the molecules of interest (decay) as well as the fragment appearance lifetimes (rise) can thus be determined, providing insight into the ultrafast photodynamics of these molecules. However, photodynamics in vacuum (and, indeed, in solution, as will be discussed further in the next section) may also follow sequential kinetics, *i.e.* different processes may not all start at $\Delta t = 0$ (see, for example, references 33 and 34). A more detailed account of laser spectroscopic techniques in the gas-phase can be found in reference 4.

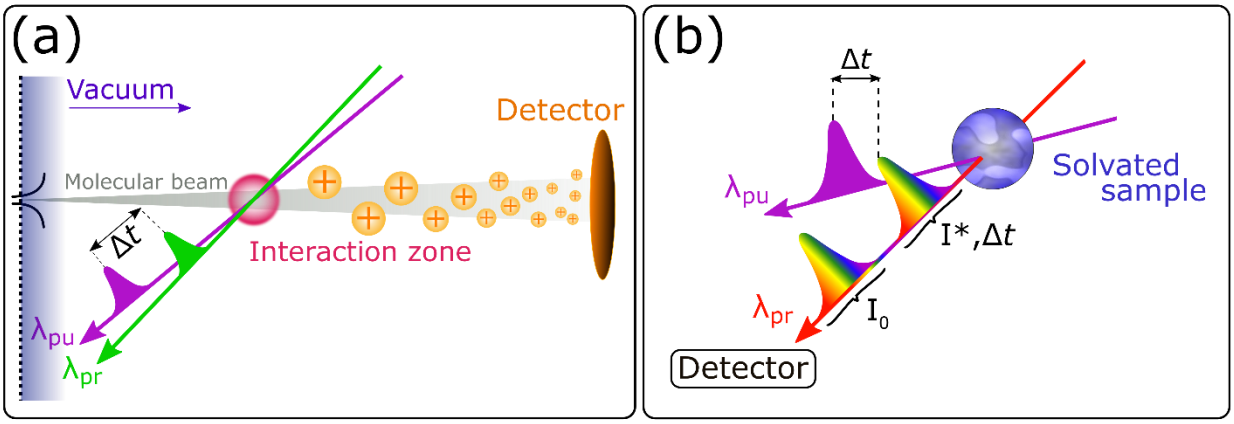


Figure 4: Diagram representation of the general experimental setups for time-resolved laser spectroscopic techniques (a) in vacuum and (b) in solution. More details regarding these techniques, including more on sample preparation/delivery and detection methods can be found in references 4 and 27, for example.

b. In solution

Pump-probe approaches have also been very successfully applied to the study of chemical reactions in solution, where the molecules of interest are solvated. As before, the sample is photoexcited by a pump laser pulse to the excited state of interest. However, in contrast with gas-phase techniques, in *transient electronic absorption spectroscopy* (TEAS) the probe pulse is a white light continuum (typically consisting of wavelengths between ~300-800 nm).[27] The photoexcited species (or resulting fragments) will then further absorb the probe wavelengths which correspond to allowed electronic transitions, effectively yielding an excited state absorption spectrum at each probe step, *i.e.* at each time delay, Δt. The spectra collected at each Δt are difference spectra, *i.e.* a logarithmic quotient of the light transmitted by the sample before (I_0) and after excitation (I^*, Δt) for each probe wavelength.[27] The final transient absorption spectra (TAS) recorded are a convolution of all the processes that have an effect on the absorption of the excited state, occurring on their individual timescales.[27] We note here, briefly, that similar experiments can be done using infrared radiation for the probe pulse. In such *transient vibrational absorption spectroscopy* (TVAS) experiments, the time evolution of vibrational modes is followed and thus dynamic structural information is obtained. TVAS will not be further discussed in this review, however; the reader is referred to reference 35 and references therein for more information and examples.

Photodynamic information about the system under study can be obtained from an analysis of typical TAS features. For example, a ground state bleach is a negative TAS feature whose evolution is a measure of how quickly the photoexcited molecule returns to its ground state. The appearance of a photoproduct may also be readily identifiable by the growth of a positive feature in the TAS. In order to deconvolute the different processes contributing to the TAS and to extract their respective time constants, the transients can be evaluated by global fitting (*i.e.* taking all probe wavelengths into account simultaneously) according to a pre-defined kinetic model.[27] This is similar to what was discussed for the gas-phase transients, but in the

case of TEAS measurements the addition of the solvent makes the kinetics more complex. If the convoluted processes are assumed to start at the same time, the dynamics are said to be *simultaneous* and the kinetic model is simply a sum of *m* exponential decays and rise functions with lifetimes τ_m (similar to gas-phase transients). However, the dynamics can also be sequential, with one process leading to the next, or even branched, for which excited state population in an intermediate state follows two or more separate relaxation pathways. The kinetic model used for fitting TAS, which is usually created based on chemical intuition and/or quantum chemical calculations, needs to be adjusted accordingly for these cases.[27] The lifetimes extracted from such an analysis can then be assigned the photophysical processes occurring in the photoexcited molecules. A more detailed description of TEAS measurements and data analysis can be found in reference 27.

It is worth noting here that, in a similar fashion to the TEAS technique just described, an emission (rather than absorption) signal can be monitored instead, yielding time-resolved emission spectra (*e.g.* to measure fluorescence lifetimes). Such an approach would then provide extra information regarding emissive states and their time-dependent behaviour. Moreover, steady absorption/emission spectroscopic techniques, *i.e.* standard Ultraviolet and Visible (UV/Vis) spectroscopy or fluorescence/phosphorescence measurements, respectively, are useful tools in the study of sunscreen photophysics.

3. Towards Optimum Photoprotection

In this section, the current literature on the ultrafast photodynamics of sunscreen molecules will be briefly reviewed. The following discussion relies strongly on a *bottom-up approach* to rational molecular design, for which the molecular complexity of the system under study is incrementally increased. Such an approach involves studying sunscreen molecules first in isolation (in vacuum) so that their intrinsic properties are understood and the effects of substituent position/functional group are evaluated. In order to understand the real-life behaviour of the active ingredients in a sunscreen formulation, solvent effects on sunscreen photodynamics then need to be explored. Pushing the current boundaries of knowledge in this field will involve studying sunscreen *mixtures* in different solvents, thin films, and, ultimately, *in vivo*. The ensuing discussion will not only review recent advances in the field of ultrafast photodynamics of sunscreens but also identify and analyse any trends emerging from the current literature on the subject. While the emphasis will be on time-resolved ultrafast spectroscopic techniques – and, in particular, in studies in solution, *i.e.* closer to the conditions in which sunscreens are used – results from other types of experiment and/or computational studies may also be evoked to inform the discussion and prompt future work.

a. Photophysical Mechanisms

As previously discussed, the photophysics of an ideal sunscreen molecule should allow for fast dissipation of excess energy as harmless heat, with no detriment to molecular integrity. In other words, a sunscreen molecule should efficiently transition from its n^{th} excited state (S_n, where $n = 1$ for the first singlet excited state, $n = 2$ for the second singlet excited state, *etc.*) to its electronic ground state (S_0). Such transitions between electronic states of the same spin multiplicity – internal conversion (IC) – can be facilitated by conical intersections (CIs). These intersections are particular points in molecular geometry where different electronic states are degenerate, allowing for excited state population to efficiently transition between them. Certain molecular motions undergone by photoexcited sunscreen molecules may drive them towards a CI with the S_0 state, thus allowing for fast relaxation to take place. The following section explores some of the molecular motions that have been found to facilitate efficient IC in sunscreen molecules.

i. Trans/Cis isomerisation

Photoisomerisation has been found to be the preferred relaxation mechanism for a family of sunscreens used in commercial formulations, the cinnamates, some of which are presented in Figure 5.[4] *Trans*-ethyl-4-hydroxy-3-methoxycinnamate (ethyl ferulate, EF), for example, was found to undergo *trans-cis*

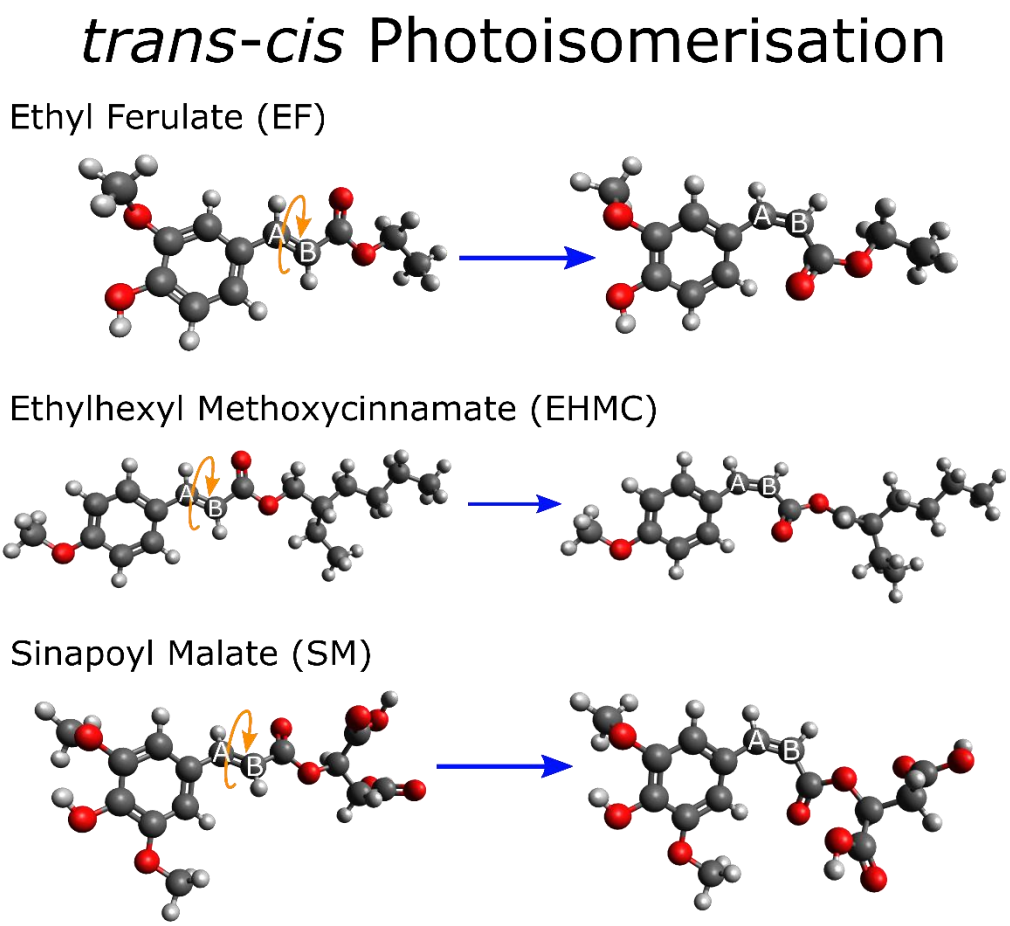


Figure 5: Representation of the isomerisation undergone by cinnamates and sinapoyl malate upon photoexcitation with UV radiation. It is this molecular motion that facilitates IC to the ground energy state in these molecules, ultimately affording them their photoprotective capabilities. It is desirable, however, that the resulting isomers retain such photoprotective capabilities and, importantly, that they are non-toxic.

photoisomerisation in a range of different solvents by Horbury *et al.*[36] Photoexcitation of EF to its first singlet excited state (S_1) was found to prompt an initial geometry relaxation followed by an evolution along the photoisomerisation coordinate. The *cis* isomer, the presence of which Horbury *et al.* confirmed by ^{1}H NMR, was observed to appear approximately 2 ps after photoexcitation and to persist for several nanoseconds, as summarised in Table 1.[36] However, Horbury *et al.* were unable to unambiguously determine how many CIs were involved in the relaxation mechanism of EF; two possible mechanisms were suggested, as shown diagrammatically in Figure 6. Similar TEAS studies by Peperstraete *et al.* on ethylhexyl methoxycinnamate (EHMC), a common ingredient in commercial sunscreen formulations, also found evidence for a relaxation mechanism by which photoexcited EHMC undergoes energy redistribution to the solvent followed by an evolution along the photoisomerisation coordinate and, finally, formation of the long-lived *cis* isomer.[37]

There is further evidence suggesting that photoisomerisation may be nature's preferred mechanism for dissipating excess energy resulting from absorption of UV radiation. *In vacuo*, frequency-resolved studies by Zwier and co-workers on sinapoyl malate (SM), the primary UVB filter in the leaves of *Brassicaceae* plants, identified the possibility for photoexcited sinapoyl malate to dissipate excess energy and return to its S_0 state *via* an efficient relaxation mechanism.[38] Subsequent time-resolved work by Baker *et al.* employed TEAS to further elucidate on the photophysical processes that follow photoexcitation of SM. These authors found that photoexcited SM undergoes an initial geometry relaxation on S_1 followed by both solvent rearrangement and IC to a second electronic state, S_2. Finally, photoisomerisation to the *cis* isomer takes place *via* an S_2/S_0 CI (timescales are summarised in Table 1;

the presence of the *cis* isomer was confirmed by comparison with post-irradiation UV/Vis spectra).[39] Interestingly, Baker *et al.* also studied the biological precursor to sinapoyl malate, sinapic acid (SA), having found no significant differences between their excited state dynamics.[39] As we will discuss in section *3.c. Environment Effects*, the explanation for nature's choice of SM instead of SA may be related to their relative performances at physiological pH, as concluded by Luo *et. al.*[40]

Table 1: Summary of the time constants extracted from TEAS measurements (parallel studies by different authors) along with their assigned process within the relaxation mechanisms of these molecules.

Molecule (author)[ref]	**τ_1 / fs** *Geometry relaxation / solvent rearrangement / energy redistribution*	**τ_2 / ps** *IC / evolution along photoisomerisation coordinate*	**τ_3 / ps** *Appearance of the* cis *isomer*	**τ_4** *Persistence of the* cis *isomer*
EF (Horbury)[36]	50 – 500	1 – 3	5 – 15	>> ns
EHMC (Peperstraete)[37]	200 – 600	–	0.7 – 2	>> ns
SM (Baker)[39]	50 – 600	1 – 5	20 – 30	>> ns

These examples highlight the importance of photoisomerisation as a mechanism by which sunscreen molecules dissipate the excess energy resulting from absorption of UV radiation. In fact, as we will see in the next section, even when sunscreen photodynamics are initially facilitated by other photophysical processes, photoisomerisation still plays a vital role in their ability to safely and effectively dissipate excess energy. It is important, however, that the resulting isomeric photoproduct is an efficient UV absorber, and hence the photodynamics of these species should also be evaluated. Moreover, it is crucial that the resulting isomer is non-toxic – something that has recently been questioned for EHMC.[41]

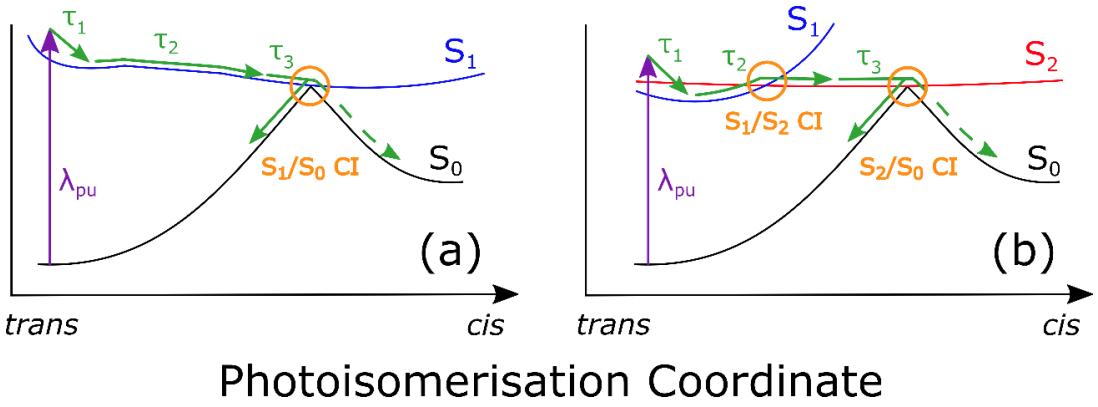


Figure 6: Representative schematic of the two relaxation mechanisms proposed for EF in reference 36. In mechanism (a) photoisomerisation occurs via an S_1/S_0 CI, while mechanism (b) proposes that an additional S_1/S_2 CI is involved in the photoisomerisation pathway. Similar mechanisms are also suggested to be responsible for the photodynamics of EHMC and SM in references 37 and 39, respectively. Adapted from reference 36.

ii. Excited State Intramolecular Proton Transfer (ESIPT) and *keto-enol* tautomerisation

Sunscreen molecules with an intramolecular hydrogen bond along which excited state proton transfer and/or tautomerisation processes may occur, such as anthranilates and salicylates, are usually referred to in sunscreen literature as 'stable' and 'safe' compounds.[25,42] While the enhanced excited state stability provided by intramolecular proton transfer (ESIPT) and *keto-enol* tautomerisation may hinder photofragmentation, the resulting (potentially) long-lived excited states are undesirable: the longer the excited state lifetimes, the higher the probability of energy transfer, from both singlet or triplet states, that may initiate harmful side photochemistry.[29,43,44] Nevertheless, there are currently marketed UV absorbers whose relaxation mechanisms are facilitated by these proton transfer processes.

One such example is avobenzone, shown in Figure 7(a), one of the most important UVA absorbers currently available on the market.[20] Avobenzone is known to exchange between its *enol* and diketo forms (*via* an *enol-keto* tautomerisation mechanism), which is thought to be the source of its undesirable photoinstability. Dunkelberger *et al.*[45] performed TEAS studies on avobenzone and modelled the resulting TAS with two time constants. The first, τ_1 ~ 0.5-1 ps, reflects the decay of the S_1 state of avobenzone into a vibrationally hot *enol* and three non-chelated *enol* (NCE) isomers of avobenzone (see Figure 7(a)).[45] Following the decay of the S_1 state, Dunkelberger *et al.* were also able to observe the vibrational relaxation of hot *enol* avobenzone occurring within ~ 6 ps.[45] In addition, the authors found evidence for three further distinct relaxation processes, which they assigned to the appearance and subsequent relaxation of the three NCE isomers of avobenzone. The yield of diketo avobenzone, known to generate triplet states and thus lead to photodegradation and ROS,[46] was found to be negligible, in accordance with previous parallel studies.[45,47]

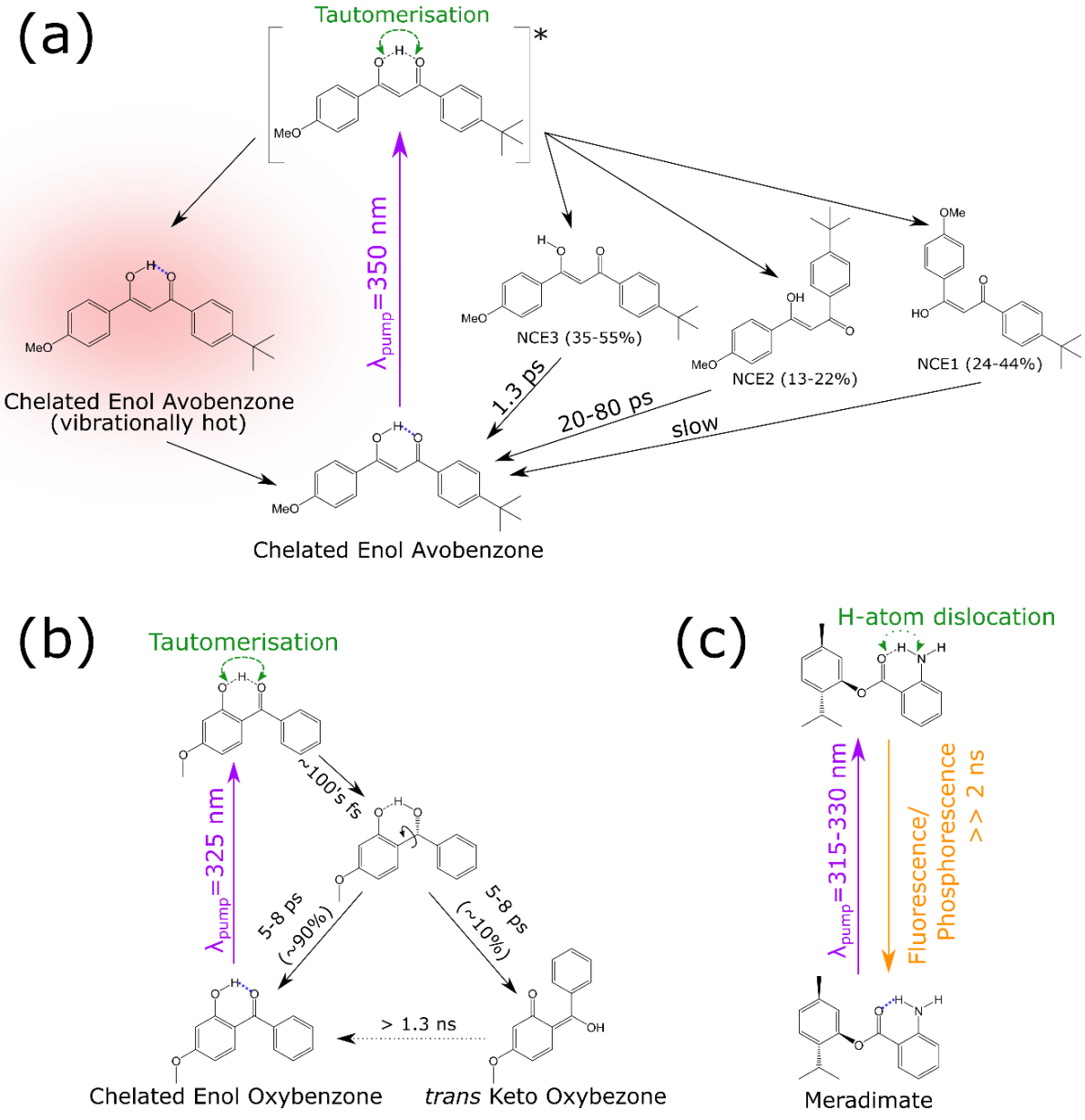


Figure 7: Different relaxation mechanisms facilitated by ESIPT/*keto-enol* tautomerisation: the examples of (a) avobenzone, (b) oxybenzone and (c) meradimate are presented. Figures adapted, respectively, from references (a) 45, (b) 48 and (c) 50.

Another example of a sunscreen molecule that undergoes *enol-keto* tautomerisation is oxybenzone, which was studied in solution by Baker *et al*.[48] In this case, migration of the intramolecularly bound hydrogen is accompanied by necessary rotational motion along the central C-C bond (see Figure 7) leading to a CI with S_0; a twisted chelated *keto* isomer is thus formed within a few hundred femtoseconds. However, the unstable chelated *keto* isomer (in S_0) quickly decays into a vibrationally hot form of the chelated *enol*, which is then observed to cool by energy transfer to the solvent within ~5-8 ps.[48] Baker *et al.* also found evidence of a photoproduct being formed upon photoexcitation of oxybenzone which, by comparison of experimental data with computational studies, the authors were able to identify as the long-lived (> 1.3 ns) *trans* keto isomer of oxybenzone, resulting from the photoisomerisation of the vibrationally hot chelated *keto* isomer (see Figure 7(b)).[48] The authors suggested a quantum yield of formation for the *trans* keto isomer of approximately 10% which could be significant if this isomer has harmful effects on the skin, however, to the best of our knowledge, this issue remains unexplored. Given this study by Baker *et al.*, oxybenzone seems a close-to-ideal sunscreen: a strong UVA/UVB absorber which dissipates energy within a few picoseconds, almost completely regenerating to its ground energetic state. However, oxybenzone is a known endocrine disruptor and, therefore, there are concerns regarding its use in commercial sunscreen formulations.[49]

Finally, we refer to the case of meradimate, an *ortho* aminobenzoate, the molecular structure of which is shown in Figure 7(c). Having studied meradimate both in vacuum and in solution, Rodrigues *et al.* have found that photoexciting this sunscreen both in the UVA (330 nm) and UVB (315 nm) regions of the electromagnetic spectrum accesses an excited state (S_1) which persists for several nanoseconds, with no significant ultrafast photophysics taking place.[50] Rodrigues *et al.* propose that the excited population of meradimate is trapped in an electronic state in which H-atom dislocation, akin to an incomplete *keto-enol* isomerisation, occurs between the amino and carbonyl groups.[50] This is in stark contrast with the case of oxybenzone, as discussed above, for which the *keto-enol* isomerisation, followed by a rotation motion, allows for quick dissipation of energy. Nevertheless, computational studies for meradimate performed by Rodrigues *et al.* revealed a nearby CI connecting the S_1 to the S_0 states along a twisting motion around the C-C bond connecting the phenyl ring and the ester substituent, akin to the relaxation mechanism of oxybenzone.[50] However, the energy barrier for this twisting motion is outside the UVA/UVB range in meradimate and thus would not be accessed in the context of normal sunscreen usage. Nevertheless, the studies by Rodrigues *et al.* suggest that if the energy barrier for this motion could be lowered by careful molecular design, then an effective relaxation pathway may be opened (akin to oxybenzone) and potentially optimum photoprotection capabilities could be achieved. This conclusion highlights the importance of evaluating the effects of molecular structure on the photodynamics of sunscreen molecules, as is explored in the next section.

b. Molecular Structure Effects

It has long been known that substitution of aromatic rings alters their electronic structure and that both the nature and position of substituents influences the molecule's photodynamics.[51-56] In addition, time-resolved techniques have previously been successfully applied to evaluate how substituent effects alter molecular relaxation dynamics of aromatic systems.[55-57] Gathering a comprehensive understanding of how substituent nature (functional group) and position may affect the relaxation mechanisms of sunscreen molecules – a discussion we aim to initiate in the following sections – may inform future design of advanced sunscreens tailor made for optimum photoprotection.

i. Functional Groups

Some molecular structural changes, despite increasing the molecular complexity quite significantly, do not alter the photo-induced ultrafast dynamics of the molecule. One such example would be the case of the precursor/sunscreen pair MMC/EHMC, as studied by Peperstraete *et al*.[37] MMC differs from EHMC in that, in place of the more complex ethylhexyl chain (in EHMC), there is only a methyl group. This

difference was found to have negligible impact on the observed photodynamics, as could perhaps be expected given the non-perturbative character of the molecular units in question (alkyl chains).[37] Substituting the ester group in ethyl ferulate (EF) by a carboxylic acid – yielding the natural compound ferulic acid (FA) – was also found to have no impact on the observed photodynamics. As for EF, the intramolecularly bound phenolic OH group does not dissociate. Moreover, while radical species (not observed for EF) were observed in FA by Horbury *et al.*, these were found to be an artefact of high laser powers and, therefore, not relevant in the context of normal sunscreen use under solar-like conditions.[58] The main relaxation pathway for FA is, therefore, virtually unchanged from the case of EF, *i.e.* photoisomerisation (*trans-cis*).[58]

A carbonyl moiety, on the other hand, has been found to have a drastic effect on the photodynamics of EF. In a gas-phase TR-IY study by Rodrigues *et al.*, EF was studied along with two of its precursors, 2-methoxy-4-vinylphenol (MVP) and 4-hydroxy-3-methoxycinnamyl alcohol (ConA).[59] The authors found that photoexcited MVP and ConA both have long-lived excited states (> 1.2 ns).[59] The addition of the alcohol unit (MVP *vs.* ConA) thus seemed to have no impact on the observed photodynamics. However, when an ester group is added in EF, the photodynamics are accelerated and the relaxation mechanism was proposed to involve triplet states and fluorescence (see section *3.c. Environment Effects* for a comparison with the mechanisms of EF in solution). The ester group was thus shown to alter the electronic structure of the molecule in such a way that it accelerated the relaxation of photoexcited EF,[59] suggesting that the ester group plays an important role in the photoprotective capabilities of cinnamates.

Finally, we explore how different substituents affect photodynamics which are mediated by *keto-enol* tautomerisations, discussed in the previous chapter. It is interesting to note that, in the case of oxybenzone, tautomerisation takes place effectively, with the H-atom being transferred to the nearby oxygen and rotation around the central C-C bond then occurring as a result.[48] In *ortho*-hydroxybenzaldehyde, studied in the gas-phase with TR-PES by Stolow and co-workers, tautomerisation was also found to occur completely, with the *keto* and *enol* isomers having well defined potential energy minima.[60] On the other hand, meradimate, in which the H-atom is exchanged between a nitrogen and an oxygen (*c.f.* two oxygens in the former examples), undergoes only an H-atom *dislocation*, rather than a complete transfer, ultimately resulting in a long-lived excited state.[50] The same conclusion had been drawn by Zwier and co-workers upon studying the carboxylic acid version of meradimate, anthranilic acid, using gas-phase frequency resolved techniques.[61] Should chelated *enol* sunscreen molecules (such as oxybenzone), then, be preferred over their amino counterparts (*e.g.* long-lived excited state meradimate)? Could meradimate be a better sunscreen if the amino group was substituted by a hydroxy group? This change would yield a compound of the salicylate family, another category of sunscreen molecules currently used in the market. Some salicylates commonly found in commercial sunscreen formulations have been shown to generate triplet states,[62] while salicylic acid has been found to be toxic when used in relatively high concentrations.[63] To the best of our knowledge, however, the ultrafast photodynamics of salicylates remains largely unreported.

These examples touch only the surface of the question of the effects of different functional groups on sunscreen photodynamics. With few studies having been carried out to date, there is not enough information to establish any behavioural trends and thus answer questions such as: are carbonyl compounds always good sunscreens? Do amino groups in tautomerising compounds always result in long-lived excited states? Given that each molecule has a specific electronic structure, which different functional groups will affect differently, establishing said trends presents itself as a monumental task. Nevertheless, being able to rationalise what functional groups tend to facilitate optimum relaxation mechanisms may prove crucial for effective sunscreen design and, therefore, further work on this topic is of the utmost importance.

ii. Substituent Positioning

While the effects of substituent positioning (*ortho*, *meta*, *para*, see Figure 8) on the electronic structure of benzene rings and thus their overall chemical behaviour is well documented,[54,55] a comprehensive understanding of how these effects alter the ultrafast photodynamics of these molecules – particularly, of the sunscreen molecules we are here discussing – is still lacking. An example of the approach required for such an understanding to be garnered is that of the studies by Promkatkaew *et al.*[64] These authors systematically studied a series of cinnamates and cinnamic acids using steady state spectroscopy – *i.e.* by measuring UV/Vis absorbance and emission spectra – accompanied by theoretical studies. While the study by Promkatkaew *et al.* did not involve time-resolved spectroscopy, it constitutes a good example of how a systematic bottom-up approach may be used in exploring substituent position effects in sunscreen molecules and thus deserves a brief mention here.

Promkatkaew *et al.* studied eighteen different cinnamates and cinnamic acids and systematically explored the effects of hydroxy, nitro and fluoro substitutions at *ortho*, *meta* and *para* positions on their photophysical properties, with particular interest in the resulting photoprotective capabilities of these molecules.[64] These authors first report on the effects of substituent position on the shapes of absorption spectra: for hydroxy derivatives, for example, *ortho*-cinnamates show two distinct absorption bands, while the analogous *meta* compounds have a single absorption band with asymmetric shoulders and the *para* compounds present single broad absorption bands.[64] The same authors also found that the nature and positions of substituents could influence relaxation pathways. It was established in their work that electron-withdrawing (nitro and fluoro) groups tend to encourage relaxation mechanisms *via* triplet states, while compounds with electron-donating (hydroxy) groups tend to decay *via* singlet excited states.[64] Promkatkaew *et al.* point out, however, that this trend is highly dependent on substituent position. For example, these authors found that *meta*-hydroxy cinnamate derivatives show significantly more emission than their *para* counterparts, suggesting that the *para* substituent position promotes non-radiative decay pathways. In addition, the authors evaluated the photostability of the species under study by measuring their absorption spectra before and after irradiation (at several time intervals) – Promkatkaew *et al.* then considered the molecule to be photostable if the absorption spectra are unchanged upon irradiation. Based on absorption and emission spectra, and on the results from this photostability analysis, Promkatkaew *et al.* conclude that *para*-hydroxy cinnamate derivatives are the best sunscreen candidates.[64]

The aforementioned studies provide valuable insight into substituent effects on the photodynamics of sunscreen molecules and their derivatives. In their paper, the authors highlight the need for corresponding time-resolved measurements to be carried out in order to understand the relaxation mechanisms of these molecules, and thus better understand substituent effects on photodynamics.[64]

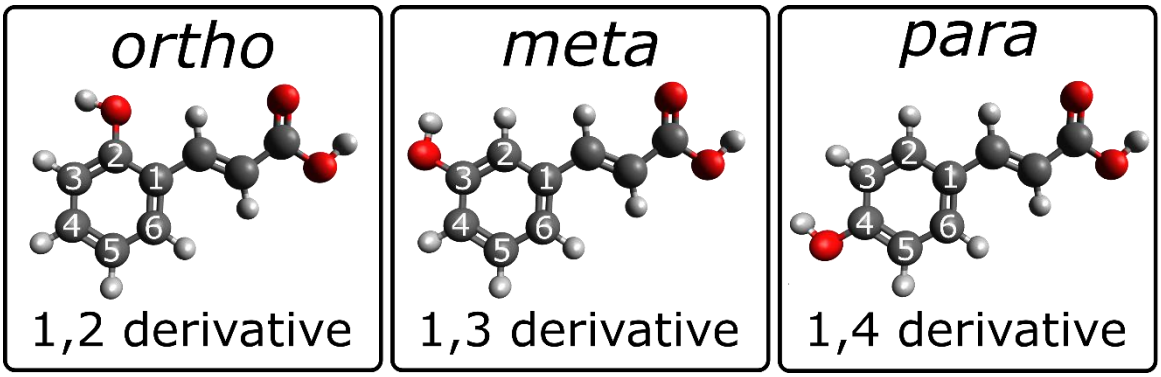


Figure 8: The *ortho*, *meta* and *para* substituent positions illustrated by the examples of some of the cinnamic acid derivatives studied by Promkatkaew *et al.*[60] These substituent positions can also be referred to in terms of numerical ordering of substituents, *i.e. ortho* compounds are substituted in positions 1 and 2, *meta* compounds are substituted in positions 1 and 3 and *para* compounds are substituted in positions 1 and 4.

Indeed, systematically studying the same eighteen species (or other such series of related molecules) with time-resolved laser spectroscopy techniques could reveal key trends in the photodynamics of differently substituted sunscreens. Such insight would expedite the molecular design of sunscreen molecules which are tailor made for optimised photoprotection.

c. Environmental Effects

It is intuitive that the surroundings of a molecule would have an effect on its electronic structure and, therefore, on its ultrafast photodynamics. Several aspects of the surroundings of a sunscreen molecule affect its chemistry, such as solvent polarity, pH and viscosity. As well as exploring how solvent factors affect the ultrafast photodynamics of sunscreen molecules, we will take a step towards the future of these studies and briefly mention what is known and what is of interest in analysing sunscreen molecules within mixtures that more closely resemble real-life sunscreen formulations.

i. Solvent (solution *vs.* vacuum)

In comparison with a molecule in isolation, a solvated molecule has a solvent "bath" into which it may dissipate excess energy. The presence of solvent can thus have a drastic impact on the observed photodynamics. In the specific case of EHMC, TR-IY (vacuum) studies by Peperstraete *et al.* revealed a long lifetime upon photoexcitation within the UVA/UVB range, assigned to a long-lived $^1n\pi^*$ state. Tan *et al.* had already observed that clustering EHMC with water resulted in this long-lived behaviour being altered.[65] Peperstraete *et al.* expanded on these studies to reveal that even a non-polar (thus minimally perturbing) solvent such as cyclohexane caused sufficient re-ordering of the excited states of EHMC so as to facilitate ultrafast photoisomerisation to occur (as discussed in *3.a. Photophysical mechanisms*).[36,37] The solvent effects in this case are evident, playing a crucial role in the suitability of EHMC for use as an efficient sunscreen. These experimental observations are in line with computational studies by Chang *et al.* which predicted significant changes in the energy barrier towards photoisomerisation in solution *vs.* in vacuum.[66]

A similar conclusion can be drawn for EF. TR-IY studies on gas-phase EF by Rodrigues *et al.* revealed a tri-exponential decay involving a long-lived, > 900 ps component, which was assigned to long-lived triplet states.[59] Apart from excited triplet state reactions such as singlet oxygen sensitising, the existence of such triplet states could be particularly problematic in sunscreen formulation since aromatic carbonyl compounds are known to undergo fragmentation reactions from their triplet states, rather than phosphorescence to the ground state.[67,68] However, as previously discussed and as observed in the studies by Horbury *et al.* on EF in solution, solvent effects – even those of the weakly perturbing cyclohexane – allow for photoisomerisation relaxation pathways to become accessible in EF, justifying its use in sunscreen formulations.[36]

It is not always the case, however, that solvents will significantly alter the gas-phase photodynamics of sunscreen molecules. As described previously (see *3.a. Photophysical mechanisms*), Rodrigues *et al.* recently observed the photodynamics of meradimate both in vacuum and solution to be long-lived (> 1.2 ns). In both cases, Rodrigues *et al.* suggested photoexcitation of meradimate to its S_1 state results in trapping of the excited state population, with no accessible CIs from this state at the pump energies used.[50] Thus, radiative decay pathways (fluorescence and phosphorescence) were suggested for meradimate in both vacuum and solution.[50] Therefore, solvent effects (at least those of cyclohexane and methanol) have been shown by Rodrigues *et al.* to not greatly affect the ultrafast photodynamics of meradimate, in contrast to what has been observed for the cinnamates.[50]

These examples highlight the complexity of solvation on ultrafast photodynamics, which remain poorly understood. This may be due to a lack of comprehensive studies focusing solely on such effects, but also to the difficulty of modelling solute-solvent interactions computationally.

ii. pH

The parallel studies by Wang *et al.* and Luo *et al.* have recently explored the effects of environment pH on the photodynamics of ferulic acid and sinapic acid/sinapoyl malate, respectively.[40,69] Wang *et al.* performed both absorption and emission time-resolved spectroscopy studies on *trans* and *cis* ferulic acid in their neutral, anionic and dianionic forms.[69] With the aid of complementary computational studies, Wang *et al.* confirmed a photoisomerisation relaxation pathway for all species studied at all pH values. These authors were also able to gather evidence for photoisomerisation occurring *via* two CIs, *i.e.* S_1/S_2 and S_2/S_0 (as shown in Figure 6(b)) in all systems studied.[69] The lifetimes were found to be comparable in all cases but one, the di-ionic form of *cis* ferulic acid (cFA^{2-}), for which photoisomerisation was found to take place within 1.4 ps (*c.f.* ~ 20 ps in all other cases). Wang *et al.* thus concluded that, for the case of cFA^{2-}, environment pH induced a change in electronic states such that photoisomerisation became barrierless, accelerating the overall decay.[69]

Luo *et al.*, on the other hand, explored the effects of pH on the photodynamics of sinapic acid (SA) and sinapoyl malate (SM), in an attempt to justify nature's choice of sinapoyl malate as a plant sunscreen.[40] As discussed earlier, in studies by Baker *et al.* it had transpired that the photodynamics of SA and SM were similar and no evidence had been found to suggest SM is a better sunscreen.[39] In recognising that the pH within a plant leaf ranges between pH = 6-8, Luo *et al.* studied the ionic forms of SA and SM, SA^- and SM^{2-}, as they occur at physiological pH.[40] Luo *et al.* confirmed photoisomerisation (both *trans* → *cis* and *cis* → *trans*) relaxation pathways for SA, SA^- and SM^{2-}, *i.e.* even when pH is taken into account, the photodynamics of these species seem to be comparable.[40] However, as Luo *et al.* concluded from steady state irradiation measurements, the photoisomerisation process for SM^{2-} (as for SA) yields a *cis* isomer which retains the absorption spectrum characteristics of the *trans* isomer, both in terms of shape and intensity. For SA^-, on the other hand, the peak of absorption of the *cis* isomer is blue-shifted and decreased in intensity when compared to *trans* SA^-.[40] The fact that the *cis* isomer resulting from photoisomerisation of the naturally occurring SM^{2-} retains good sunscreen capabilities, while that of SA^- does not, could explain nature's choice of SM for a plant sunscreen.[40]

These studies serve as examples of how pH may influence sunscreen photodynamics. Importantly, they also highlight the need to consider the pH of the environment in which sunscreens are employed, as this may alter their photophysical behaviour.

iii. Viscosity

Early studies by Espagne *et al.* explored the influence of solvent viscosity on the absorption and emission spectra of *para*-hydroxycinnamates, and found the timescales for photoisomerisation in the *p*-hydroxycinnamates to be largely unaffected by solvent viscosity.[70] If photoisomerisation was facilitated by an out-of-plane rotation around the C=C bond, the large amplitude nuclear motion would have been affected by solvent viscosity. The authors suggest, therefore, that the photoisomerisation of *p*-hydroxycinnamates occurs instead along a lower amplitude in-plane twisting motion,[70] which has been separately confirmed in recent studies.[71] On the other hand, TEAS measurements by Horbury *et al.* on sinapoyl malate (SM) have found that the time constant assigned by the authors to evolution of the excited state population along the *trans-cis* photoisomerisation increases significantly with increasing viscosity.[72] Specifically, photoisomerisation of SM dissolved in ethanol, ethylene glycol and glycerol (in order of increasing viscosity) takes 47 ps, 188 ps and 560 ps, respectively.[72] Horbury *et al.* therefore conclude that photoisomerisation of SM likely involves out-of-plane rotation about the C=C bond and, therefore, solvent viscosity has a large effect on its photodynamics.[72]

The aforementioned studies are not only the first steps towards understanding how viscosity affects sunscreen photodynamics, but they also provided more detail on the molecular motions involved in photoisomerisation relaxation pathways. The effects of viscosity on the photodynamics of sunscreen molecules remain, nevertheless, largely unexplored.

iv. Mixtures

So far, we have considered the photodynamics of sunscreen molecules either in vacuum or in contact with a single solvent. In reality, however, commercial sunscreens do not consist of single molecules dissolved in one solvent: sunscreen formulations are complex mixtures of several sunscreens, emollients, stabilisers, solvents, *etc*. Therefore, it is necessary to extend on the aforementioned studies and consider how sunscreen molecules affect *each other's* photodynamics.

An example of one such study is the work by Baker *et al.* on a mixture of oxybenzone and titanium dioxide (TiO_2), spanning a range of solute ratios, including those observed in commercial sunscreen lotions.[73] The authors evaluated the photodynamics of each component individually: oxybenzone, as had been observed previously, undergoes *enol-keto* tautomerisation followed by rotation around the aliphatic C–C bond which either facilitates IC to the ground state or results in isomerisation to a *trans-keto* conformation of oxybenzone (see discussion above).[48,73] Despite being used in sunscreens mainly to scatter UV radiation, TiO_2 was found in the studies by Baker *et al.* to undergo ultrafast (femtosecond, within instrument response) photodynamics when in low concentrations; at higher concentrations TiO_2 is long-lived.[73] The TEAS measurements for the mixture of these two sunscreen molecules in different solvents is simply the addition of individual spectra, with the time constants extracted matching those from the individual photodynamics.[73] Given this observation, Baker *et al.* concluded that there is minimal interaction between oxybenzone and TiO_2, and that the presence of either of them in a solvated mixture does not affect the photodynamics of the other.[73]

When the mixture is composed of two or more chemical sunscreens, however, long-lived triplet states may facilitate energy transfer between two molecules. Matsumoto *et al.*[74] explored this possibility by evaluating the ability of EHMC and octocrylene to quench the triplet states of meradimate.[50,74,75] By comparing the lifetimes of an energy donor (in this case, meradimate) as the concentration of an energy acceptor (EHMC or octocrylene) is changed in the sunscreen mixture, the authors determined the rate of triplet-triplet energy transfer between each pair of molecules, *i.e.* meradimate-EHMC or meradimate-octocrylene.[74] Matsumoto *et al.* found that the triplet-triplet energy transfer between these molecules is an extremely efficient, diffusion controlled process. In fact, Matsumoto *et al.* found that both EHMC and octocrylene quench the triplet states of meradimate at much higher rates than those observed for quenching of meradimate by oxygen.[74] While these results may suggest that EHMC and octocrylene could act as meradimate stabilisers in sunscreen formulations, it is important to evaluate if, for these and other combinations of sunscreens, energy transfer processes promote harmful chemical reactions which lead to undesirable by-products. Continued efforts towards understanding interactions between sunscreen molecules, and their impact on the resulting photodynamics, are necessary.

4. Conclusion and Outlook

With the development of ultrafast laser spectroscopic techniques, many exciting avenues of research became possible, with the understanding of the photodynamics of a plethora of systems – such as sunscreen molecules – now being within reach. While the field of ultrafast photodynamics of sunscreen molecules is relatively new, the promising results achieved in early studies have sparked the interest of the scientific community and, in fact, of the sunscreen industry. Therefore, research into the ultrafast mechanisms that allow sunscreen molecules to dissipate excess absorbed energy into harmless heat is currently receiving significant attention. Common behaviours and trends are starting to emerge, as described in this review article, such as the photoisomerisation of the cinnamates, the excited state proton transfer mechanisms taking place in sunscreens with an intramolecular hydrogen bond, and the solvent factors that have an impact on photodynamics. However, much more work needs to be done in order to systematically evaluate the impact of changing molecular structures and of the environment surrounding sunscreen molecules on their photodynamics.

In gaining such comprehensive understanding, a *bottom-up approach* has proved (and will continue to prove) crucial: studying molecules in isolation, changing substituent nature and position, increasing molecular complexity, then introducing solvents of different polarities, pH, viscosity, and, eventually, studying sunscreen molecules as part of increasingly more complex mixtures, in thin films (higher interaction between molecules) and, finally, *in vivo* (exploring how the skin environment may alter sunscreen photodynamics). Undergoing such extensive studies to the many different sunscreen molecules currently on the market, and all the others that may thus come to light, presents itself as a promisingly prolific and exciting avenue of research. In achieving a comprehensive understanding of the ultrafast photodynamics taking place in photoexcited sunscreen molecules, one hopes to unveil the key to photoprotection and hence be able to target molecular design of a new generation of sunscreens, tailor made for optimum photoprotection.

Acknowledgements

The authors would like to thank Zivani Varanaraja and Georgie Taylor for providing the UV/Vis spectra shown in Figure 2. N.d.N.R. thanks the EPSRC for doctoral funding. V.G.S. thanks the EPSRC for equipment grants (EP/J007153 and EP/N010825) and the Royal Society and Leverhulme Trust for a Royal Society Leverhulme Trust Senior Research Fellowship.

References

1. A. A. Lacis and J. Hansen, *Journal of the Atmospheric Sciences*, 1974, **31**, 118-133.
2. J. E. Frederick, H. E. Snell and E. K. Haywood, *Photochemistry and Photobiology*, 1989, **50**, 443-450.
3. National Renewable Energy Laboratory (NREL), http://rredc.nrel.gov/solar/spectra/am1.5, (accessed 16 October, 2017).
4. N. D. Rodrigues, M. Staniforth and V. G. Stavros, Proceedings of the Royal Society A, 2016, **472**, 20160677.
5. R. E. Blankenship, *Molecular Mechanisms of Photosynthesis*, Blackwell Science, Abingdon, 2002.
6. M. F. Holick, *The New England Journal of Medicine*, 2007, **357**, 266-281.
7. M. Brenner and V. J. Hearing, *Photochemistry and Photobiology*, 2008, **84**, 539-549.
8. P. Pludowski, M. F. Holick, S. Pilz, C. L. Wagner, B. W. Hollis, W. B. Grant, Y. Shoenfeld, E. Lerchbaum, D. J. Llewellyn, K. Kienreich and M. Soni, *Autoimmunity Reviews*, 2013, **12**, 976-989.
9. S. Kataria, A. Jajoo and K. N. Guruprasad, *Journal of Photochemistry and Photobiology B*, 2014, **137**, 55-66.
10. B. L. Diffey, *Physics in Medicine and Biology*, 1991, **36**, 299-328.
11. Y. Matsumura and H. N. Ananthaswamy, *Toxicology and Applied Pharmacology*, 2004, **195**, 298-308.
12. J. A. Lo and D. E. Fisher, *Science*, 2014, **346**, 945-949.
13. T. Iyama and D. M. Wilson, *DNA Repair*, 2013, **12**, 620-636.
14. D. E. Brash, *Photochemistry and Photobiology*, 2015, **91**, 15-26.
15. J. P. Lacour, *British Journal of Dermatology*, 2002, **146**, 17-19.
16. C. Battie, S. Jitsukawa, F. Bernerd, S. Del Bino, C. Marionnet and M. Verschoore, *Experimental Dermatology*, 2014, **23(1)**, 7-12.
17. F. Poon, S. Kang and A. L. Chien, *Photodermatology, Photoimmunology & Photomedicine*, 2015, **31**, 65-74.
18. B. A. Gilchrest and M. S. Eller, *Journal of Investigative Dermatology Symposium Proceedings*, 1999, **4**, 35-40.
19. M. S. Eller and B. A. Gilchrest, *Pigment Cell Research*, 2000, **13**, 94-97.
20. S. Q. Wang and H. W. Lim, *Principles and Practice of Photoprotection*, ADIS, Switzerland, 2016.
21. S. Q. Wang and H. W. Lim, *Journal of the American Academy of Dermatology*, 2011, **65**, 863-869.

22. M. Loden, H. Beitner, H. Gonzalez, D. W. Edstrom, U. Akerstrom, J. Austad, I. Buraczewska-Norin, M. Matsson and H. C. Wulf, *British Journal of Dermatology*, 2011, **165**, 255-262.
23. G. Verheugen, *Commission Recommendation on the Efficacy of Sunscreen Products and the Claims made relating thereto*, European Commission, Brussels, 2006.
24. J. R. Abney and B. A. Scalettar, *Journal of Chemical Education*, 1998, **75(6)**, 757-760.
25. R. Jansen, U. Osterwalder, S. Q. Wang, M. Burnett and H. W. Lim, *Journal of the American Academy of Dermatology*, 2013, **69(6)**, 867 e861-814; quiz 881-862.
26. F. P. Gasparro, *Sunscreen Photobiology: Molecular, Cellular and Physiological Aspects*, Springer, Berlin, 1997.
27. L. A. Baker and V. G. Stavros, *Science Progress*, 2016, **99**, 282-311.
28. J. F. Nash and P. R. Tanner, *Photodermatology, Photoimmunology & Photomedicine*, 2014, **30**, 88-95.
29. G. T. Wondrak, in *Fundamentals of Cancer Prevention*, ed. D. S. Alberts and L. M. Hess, Springer, Berlin, 3rd edn, 2014, ch. 11, pp. 301-320.
30. R. Losantos, I. Funes-Ardoiz, J. Aguilera, E. Herrera-Ceballos, C. Garcia-Iriepa, P. J. Campos and D. Sampedro, *Angewandte Chemie International Edition in English*, 2017, **56**, 2632-2635.
31. A. H. Zewail, *Science*, 1988, **242**, 1645-1653.
32. R. E. Smalley, L. Wharton and D. H. Levy, *Accounts of Chemical Research*, 2002, **10**, 139-145.
33. J. O. F. Thompson, L. B. Klein, T. I. Sølling, M. J. Paterson and D. Townsend, *Chemical Science*, 2016, **7**, 1826-1839.
34. A. S. Chatterley, G. M. Roberts and V. G. Stavros, *The Journal of Chemical Physics*, 2013, **139**, 034318.
35. E. T. Nibbering, H. Fidder and E. Pines, *Annual Review of Physical Chemistry*, 2005, **56**, 337-367.
36. M. D. Horbury, L. A. Baker, N. D. N. Rodrigues, W. D. Quan and V. G. Stavros, *Chemical Physics Letters*, 2017, **673**, 62-67.
37. Y. Peperstraete, M. Staniforth, L. A. Baker, N. D. Rodrigues, N. C. Cole-Filipiak, W. D. Quan and V. G. Stavros, *Physical Chemistry Chemical Physics*, 2016, **18**, 28140-28149.
38. J. C. Dean, R. Kusaka, P. S. Walsh, F. Allais and T. S. Zwier, Journal of the American Chemical Society, 2014, **136**, 14780-14795.
39. L. A. Baker, M. D. Horbury, S. E. Greenough, F. Allais, P. S. Walsh, S. Habershon and V. G. Stavros, *The Journal of Physical Chemistry Letters*, 2016, **7**, 56-61.
40. J. Luo, Y. Liu, S. Yang, A. L. Flourat, F. Allais and K. Han, *The Journal of Physical Chemistry Letters*, 2017, **8**, 1025-1030.
41. A. Necasova, K. Banyiova, J. Literak and P. Cupr, *Environmental Toxicology*, 2017, **32**, 569-580.
42. N. J. Lowe, *Sunscreens: Development, Evaluation and Regulatory Aspects*, Marcel Dekker, Inc., New York, 1990.
43. A. Kikuchi, N. Oguchi-Fujiyama, K. Miyazawa and M. Yagi, *Photochemistry and Photobiology*, 2014, **90**, 511-516.
44. S. Forestier, *Journal of the American Academy of Dermatology*, 2008, **58**, S133-138.
45. A. D. Dunkelberger, R. D. Kieda, B. M. Marsh and F. F. Crim, *The Journal of Physical Chemistry A*, 2015, **119**, 6155-6161.
46. J. Kockler, M. Oelgemöller, S. Robertson and B. D. Glass, *Journal of Photochemistry and Photobiology C: Photochemistry Reviews*, 2012, **13**, 91-110.
47. M. Yamaji and M. Kida, *The Journal of Physical Chemistry A*, 2013, **117**, 1946-1951.
48. L. A. Baker, M. D. Horbury, S. E. Greenough, P. M. Coulter, T. N. Karsili, G. M. Roberts, A. J. Orr-Ewing, M. N. Ashfold and V. G. Stavros, *The Journal of Physical Chemistry Letters*, 2015, **6**, 1363-1368.
49. K. L. Kinnberg, G. I. Petersen, M. Albrektsen, M. Minghlani, S. M. Awad, B. F. Holbech, J. W. Green, P. Bjerregaard and H. Holbech, *Environmental Toxicology and Chemistry*, 2015, **34**, 2833-2840.
50. N. D. N. Rodrigues, N. C. Cole-Filipiak, M. D. Horbury, M. Staniforth, T. N. V. Karsili, Y. Peperstraete and V. G. Stavros, *Journal of Photochemistry and Photobiology A: Chemistry*, 2018, **353**, 376-384.
51. G. Porter and P. Suppan, *Transactions of the Faraday Society*, 1965, **61**, 1664-1673.
52. R. N. Jones, *Journal of the American Chemical Society*, 1945, **67**, 2127-2150.
53. P. E. Stevenson, *Journal of Molecular Spectroscopy*, 1965, **18**, 51-58.

54. T. N. V. Karsili, A. M. Wenge, S. J. Harris, D. Murdock, J. N. Harvey, R. N. Dixon and M. N. R. Ashfold, *Chemical Science*, 2013, **4**, 2434-2446.
55. G. A. Pino, A. N. Oldani, E. Marceca, M. Fujii, S. I. Ishiuchi, M. Miyazaki, M. Broquier, C. Dedonder and C. Jouvet, The Journal of Chemical Physics, 2010, **133**, 124313.
56. R. Hermann, G. R. Mahalaxmi, T. Jochum, S. Naumov and O. Brede, *The Journal of Physical Chemistry A*, 2002, **106**, 2379-2389.
57. S. H. Lee, K. C. Tang, I. C. Chen, M. Schmitt, J. P. Shaffer, T. Schultz, J. G. Underwood, M. Z. Zgierski and A. Stolow, *The Journal of Physical Chemistry A*, 2002, **106**, 8979-8991.
58. M. D. Horbury, L. A. Baker, W. D. Quan, S. E. Greenough and V. G. Stavros, *Physical Chemistry Chemical Physics*, 2016, **18**, 17691-17697.
59. N. D. Rodrigues, M. Staniforth, J. D. Young, Y. Peperstraete, N. C. Cole-Filipiak, J. R. Gord, P. S. Walsh, D. M. Hewett, T. S. Zwier and V. G. Stavros, *Faraday Discussions*, 2016, **194**, 709-729.
60. S. Lochbrunner, T. Schultz, M. Schmitt, J. P. Shaffer, M. Z. Zgierski and A. Stolow, *The Journal of Chemical Physics*, 2001, **114**, 2519-2522.
61. C. A. Southern, D. H. Levy, G. M. Florio, A. Longarte and T. S. Zwier, *The Journal of Physical Chemistry A*, 2003, **107**, 4032-4040.
62. K. Sugiyama, T. Tsuchiya, A. Kikuchi and M. Yagi, *Photochemistry and Photobiology Sciences*, 2015, **14**, 1651-1659.
63. R. K. Madan and J. Levitt, *Journal of the American Academy of Dermatology*, 2014, **70**, 788-792.
64. M. Promkatkaew, S. Suramitr, T. Karpkird, S. Wanichwecharungruang, M. Ehara and S. Hannongbua, *Photochemistry and Photobiology Sciences*, 2014, **13**, 583-594.
65. E. M. Tan, M. Hilbers and W. J. Buma, *The Journal of Physical Chemistry Letters*, 2014, **5**, 2464-2468.
66. X. P. Chang, C. X. Li, B. B. Xie and G. Cui, *The Journal of Physical Chemistry A*, 2015, **119**, 11488-11497.
67. X. Cai, P. Cygon, B. Goldfuss, A. G. Griesbeck, H. Heckroth, M. Fujitsuka and T. Majima, *Chemistry: A European Journal*, 2006, **12(17)**, 4662-4667.
68. J. C. Scaiano, E. A. Lissi and M. V. Encina, *Reviews of Chemical Intermediates*, 1978, **2**, 139-196.
69. S. Wang, S. Schatz, M. C. Stuhldreier, H. Bohnke, J. Wiese, C. Schroder, T. Raeker, B. Hartke, J. K. Keppler, K. Schwarz, F. Renth and F. Temps, *Physical Chemistry Chemical Physics*, 2017, **19**, 30683-30694.
70. A. Espagne, D. H. Paik, P. Changenet-Barret, M. M. Martin and A. H. Zewail, *ChemPhysChem*, 2006, **7**, 1717-1726.
71. H. Kuramochi, S. Takeuchi and T. Tahara, *The Journal of Physical Chemistry Letters*, 2012, **3**, 2025-2029.
72. M. D. Horbury, W. D. Quan, A. L. Flourat, F. Allais and V. G. Stavros, *Physical Chemistry Chemical Physics*, 2017, **19**, 21127-21131.
73. L. A. Baker, L. C. Grosvenor, M. N. R. Ashfold and V. G. Stavros, *Chemical Physics Letters*, 2016, **664**, 39-43.
74. S. Matsumoto, R. Kumasaka, M. Yagi and A. Kikuchi, *Journal of Photochemistry and Photobiology A: Chemistry*, 2017, **346**, 396-400.
75. A. Kikuchi, K. Shibata, R. Kumasaka and M. Yagi, *Photochemistry and Photobiology Sciences*, 2013, **12**, 246-253.